Alice P. Taylor, PhD

Placental Growth Factor Regulation during Tumor Recovery

[This project will investigate how placental growth factor is expressed and participates in the recurrence of tumors after treatment.]

Despite surgical, radiation or chemotherapeutic treatment, malignant tumors recur in greater than 35% of cases depending on tumor type, size and location. Tumor regrowth after tumor cell killing treatment may depend on reestablishment of a rich blood supply to the few surviving tumor cells. Study of tumor blood supply has focused only on how the tumor becomes established or how the blood supplies the tumor's abnormal growth demands, but not on how blood supply is re-established after treatment. Yet a robust blood supply may be needed for tumors to regrow. In order to address the role of renewed tumor blood vessels in recurrence, we studied the regulation of specific vessel growth factors in 4 human tumors growing in mice. Three of the tumors were colon cancer and one was a lung tumor. The treatment used, radioimmunotherapy (RAIT), which destroys tumor cells specifically, and also much of the blood supply network in the tumor. In these tumor models, the tumors stop growing after treatment, but at 4-6 weeks after one RAIT treatment, they begin to grow again. During the time of growth arrest (week 1 to weeks 4 or 6), we examined tumor specimens for expression of blood vessel growth factors. We found that the most commonly studied growth factor, vascular endothelial growth factor (VEGF), was increased in only 1 of the tumors during renewal of the blood supply network. So we looked for other blood vessel growth factors, and found that a growth factor similar to VEGF in function, placental growth factor (PIGF), was highly expressed in 3 of 4 tumors. PIGF is normally not expressed in colon or lung tissue, so its expression in the recovering tumor is abnormal. In addition, PIGF expression is usually turned off when tissue lacks oxygen, but in these tumors, PIGF expression is heaviest where the tumor tissue lacks oxygen. For this proposal, we plan to analyze the expression of PIGF in treated tumors and compare the findings to regulation of its expression in tissue normally expressing PIGF and in untreated tumors. The findings will help us understand how PIGF may contribute to recurrence of tumors after treatment.